CLAIMS

What is claimed is:

1. A compound of Formula I

$$R^1—Q—D—(V^1)_t—R^2 \qquad I$$

or a pharmaceutically acceptable salt thereof,

wherein:

R^1 and R^2 independently are selected from:

C_1-C_6 alkyl;

Substituted C_1-C_6 alkyl;

C_2-C_6 alkenyl;

Substituted C_2-C_6 alkenyl;

C_2-C_6 alkynyl;

Substituted C_2-C_6 alkynyl;

C_3-C_6 cycloalkyl;

Substituted C_3-C_6 cycloalkyl;

C_3-C_6 cycloalkyl-(C_1-C_6 alkylenyl);

Substituted C_3-C_6 cycloalkyl-(C_1-C_6 alkylenyl);

3- to 6-membered heterocycloalkyl;

Substituted 3- to 6-membered heterocycloalkyl;

3- to 6-membered heterocycloalkyl-(C_1-C_6 alkylenyl);

Substituted 3- to 6-membered heterocycloalkyl-(C_1-C_6 alkylenyl);

Phenyl-(C_1-C_6 alkylenyl);

Substituted phenyl-(C_1-C_6 alkylenyl);

Naphthyl-(C_1-C_6 alkylenyl);

Substituted naphthyl-(C_1-C_6 alkylenyl);

5-, 6-, 9-, and 10-membered heteroaryl-(C_1-C_6 alkylenyl);

Substituted 5-, 6-, 9-, and 10-membered heteroaryl-(C_1-C_6 alkylenyl);

Phenyl;

Substituted phenyl;

Naphthyl;

Substituted naphthyl;

5-, 6-, 9-, and 10-membered heteroaryl;

Substituted 5-, 6-, 9-, and 10-membered heteroaryl;

R^3O-(C_1-C_6 alkylenyl);

Substituted R^3O-(C_1-C_6 alkylenyl);

Phenyl-O-(C_1-C_8 alkylenyl);

Substituted phenyl-O-(C_1-C_8 alkylenyl);

Phenyl-S-(C_1-C_8 alkylenyl);

Substituted phenyl-S-(C_1-C_8 alkylenyl);

Phenyl-S(O)-(C_1-C_8 alkylenyl);

Substituted phenyl-S(O)-(C_1-C_8 alkylenyl);

Phenyl-$S(O)_2$-(C_1-C_8 alkylenyl); and

Substituted phenyl-$S(O)_2$-(C_1-C_8 alkylenyl);

wherein R^1 and R^2 are not both selected from:

C_1-C_6 alkyl;

C_2-C_6 alkenyl;

C_2-C_6 alkynyl; and

C_3-C_6 cycloalkyl;

Each R^3 independently is selected from:

H;

C_1-C_6 alkyl;

Substituted C_1-C_6 alkyl;

C_3-C_6 cycloalkyl;

Substituted C_3-C_6 cycloalkyl;

Phenyl-(C_1-C_6 alkylenyl);

Substituted phenyl-(C_1-C_6 alkylenyl);

Naphthyl-(C_1-C_6 alkylenyl);

Substituted naphthyl-(C_1-C_6 alkylenyl);

5-, 6-, 9-, and 10-membered heteroaryl-(C_1-C_6 alkylenyl);

Substituted 5-, 6-, 9-, and 10-membered heteroaryl-(C_1-C_6 alkylenyl);

Phenyl;

Substituted phenyl;

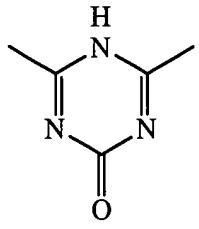
Naphthyl;

Substituted naphthyl;

5-, 6-, 9-, and 10-membered heteroaryl;

Substituted 5-, 6-, 9-, and 10-membered heteroaryl;

D is a heteromonocyclic diradical: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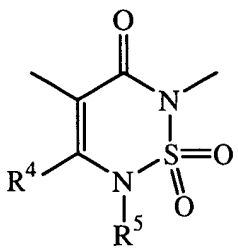
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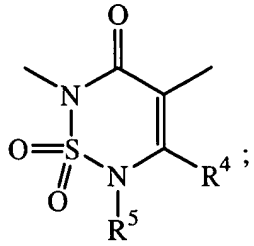
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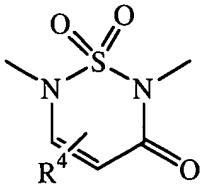
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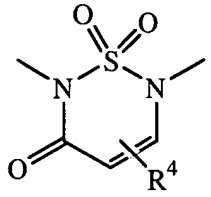
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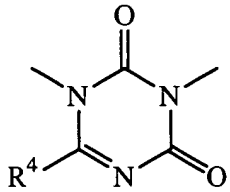
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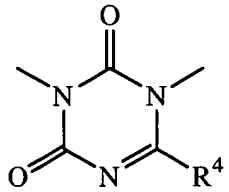
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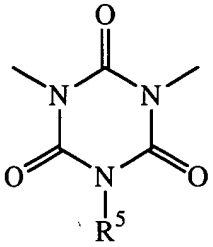
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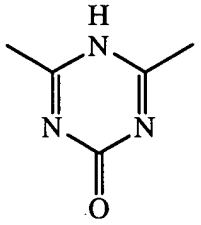
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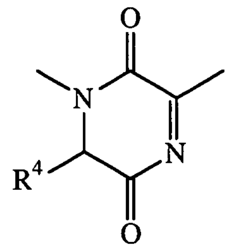
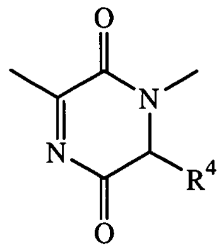
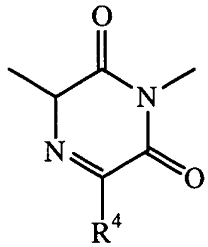
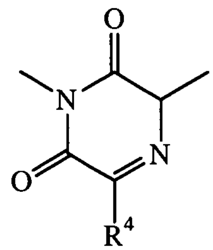
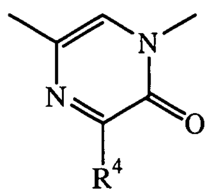
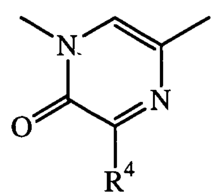
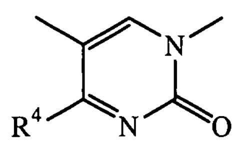
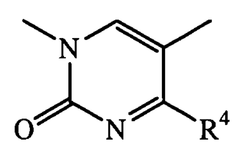
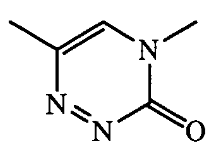
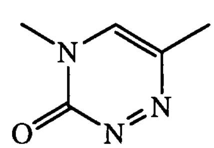
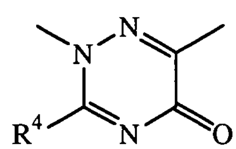
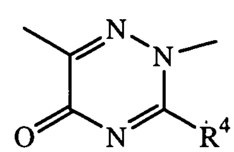
 ;  ;

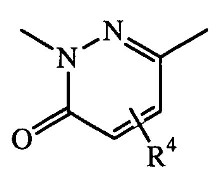
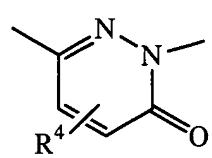
 ;  ;

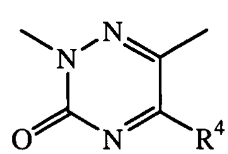
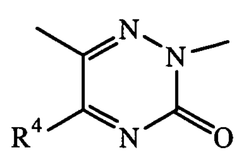
 ;  ;

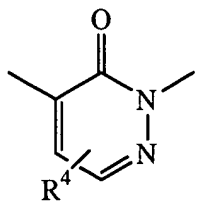
 ;  ;

 ;  ;

 ;  ;

 ;  ;

 ;  ;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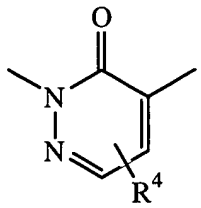
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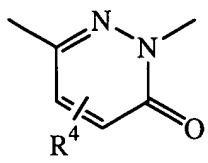
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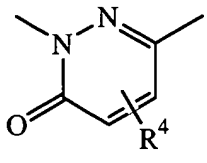

;

Each R^4 independently is selected from:

H;

F;

CH_3;

CF_3;

C(O)H;

CN;

HO;

CH_3O;

$C(F)H_2O$;

$C(H)F_2O$; and

CF_3O;

t is an integer of 0 or 1;

V^1 is selected from:

a 5-membered heteroarylenyl;

$CH_2C{\equiv}C$;

$CF_2C\ C{\equiv}C$;

C(O)O;

C(S)O;

$C(O)N(R^5)$; and

$C(S)N(R^5)$;

Q, when bonded to a nitrogen atom in group D, is selected from:

OC(O);

$CH(R^6)C(O)$;

$OC(NR^6)$;

$CH(R^6)C(NR^6)$;

$N(R^6)C(O)$;

$N(R^6)C(S)$;

$N(R^6)C(NR^6)$;

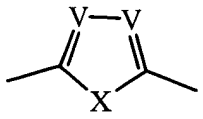
$SC(O)$;

$CH(R^6)C(S)$;

$SC(NR^6)$;

$C{\equiv}CCH_2$;

$C{\equiv}CCF_2$;



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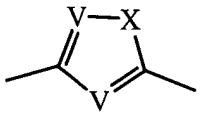

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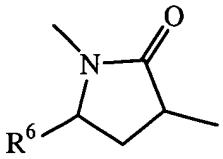

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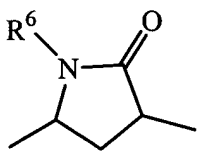

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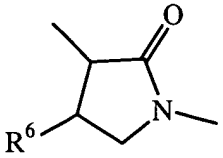

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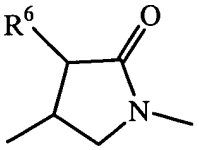

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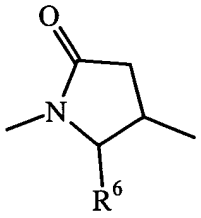


; and

Q, when bonded to a carbon atom in group D, is as defined above and may further be selected from:

OCH_2;

$N(R^6)CH_2$;

trans-(H)C=C(H);

cis-(H)C=C(H);

C≡C;

$CH_2C{\equiv}C$; and

$CF_2C{\equiv}C$;

Each X independently is O, S, N(H), or $N(C_1\text{-}C_6$ alkyl);

Each V independently is C(H) or N;

Each R^5 independently is H or $C_1\text{-}C_6$ alkyl;

R^6 is H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl; 3- to 6-membered heterocycloalkyl; phenyl; benzyl; or 5- or 6-membered heteroaryl;

Each "substituted" group contains from 1 to 4 substituents, each independently on a carbon or nitrogen atom, independently selected from:

C_1-C_6 alkyl;

C_2-C_6 alkenyl;

C_2-C_6 alkynyl;

C_3-C_6 cycloalkyl;

C_3-C_6 cycloalkylmethyl;

Phenyl;

Phenylmethyl;

3- to 6-membered heterocycloalkyl;

3- to 6-membered heterocycloalkylmethyl;

cyano;

CF_3;

(C_1-C_6 alkyl)-OC(O);

$HOCH_2$;

(C_1-C_6 alkyl)-OCH_2;

H_2NCH_2;

(C_1-C_6 alkyl)-$N(H)CH_2$;

(C_1-C_6 alkyl)$_2$-NCH_2;

$N(H)_2C(O)$;

(C_1-C_6 alkyl)-N(H)C(O);

(C_1-C_6 alkyl)$_2$-NC(O);

$N(H)_2C(O)N(H)$;

(C_1-C_6 alkyl)-N(H)C(O)N(H);

$N(H)_2C(O)N(C_1$-C_6 alkyl);

(C_1-C_6 alkyl)-N(H)C(O)N(C_1-C_6 alkyl);

(C_1-C_6 alkyl)$_2$-NC(O)N(H);

(C_1-C_6 alkyl)$_2$-NC(O)N(C_1-C_6 alkyl);

$N(H)_2C(O)O$;

(C_1-C_6 alkyl)-N(H)C(O)O;

$(C_1\text{-}C_6\ alkyl)_2\text{-}NC(O)O$;

HO;

$(C_1\text{-}C_6\ alkyl)\text{-}O$;

CF_3O;

$CF_2(H)O$;

$CF(H)_2O$;

H_2N;

$(C_1\text{-}C_6\ alkyl)\text{-}N(H)$;

$(C_1\text{-}C_6\ alkyl)_2\text{-}N$;

O_2N;

$(C_1\text{-}C_6\ alkyl)\text{-}S$;

$(C_1\text{-}C_6\ alkyl)\text{-}S(O)$;

$(C_1\text{-}C_6\ alkyl)\text{-}S(O)_2$;

$(C_1\text{-}C_6\ alkyl)_2\text{-}NS(O)_2$;

$(C_1\text{-}C_6\ alkyl)\text{-}S(O)_2\text{-}N(H)\text{-}C(O)\text{-}(C_1\text{-}C_8\ alkylenyl)_m$; and

$(C_1\text{-}C_6\ alkyl)\text{-}C(O)\text{-}N(H)\text{-}S(O)_2\text{-}(C_1\text{-}C_8\ alkylenyl)_m$;

wherein each substituent on a carbon atom may further be independently selected from:

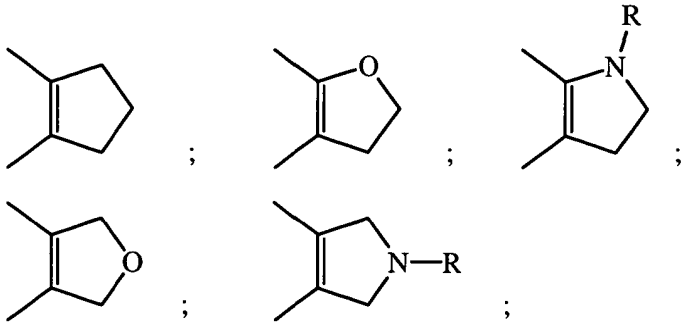
Halo;

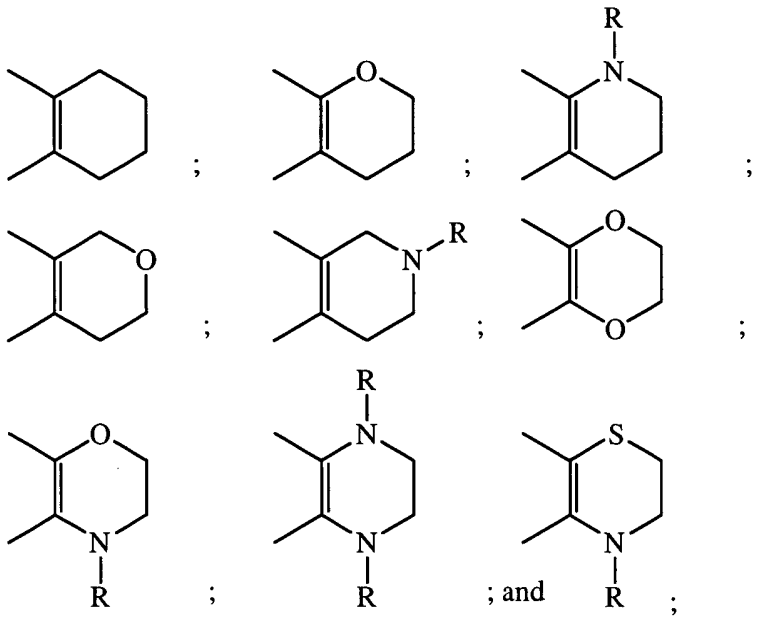
HO_2C; and

OCH_2O, wherein each O is bonded to adjacent carbon atoms to form a 5-membered ring;

wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group C=O;

wherein two adjacent, substantially sp^2 carbon atoms may be taken together with a diradical substituent to form a cyclic diradical selected from:





Each m independently is an integer of 0 or 1;

R is H or C_1-C_6 alkyl;

wherein each 5-membered heteroarylenyl independently is a 5-membered ring containing carbon atoms and from 1 to 4 heteroatoms selected from 1 O, 1 S, 1 NH, 1 N(C_1-C_6 alkyl), and 4 N, wherein the O and S atoms are not both present, and wherein the heteroarylenyl may optionally be unsubstituted or substituted with 1 substituent selected from fluoro, methyl, hydroxy, trifluoromethyl, cyano, and acetyl;

wherein each heterocycloalkyl is a ring that contains carbon atoms and 1 or 2 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 $S(O)_2$, 1 N, 2 N(H), and 2 N(C_1-C_6 alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond;

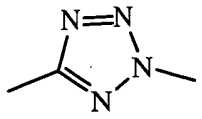
wherein each 5-membered heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C_1-C_6 alkyl), and 4 N, and each 6-membered heteroaryl contains carbon atoms and 1 or 2 heteroatoms independently selected from N, N(H), and N(C_1-C_6 alkyl), and 5- and 6-membered heteroaryl are monocyclic rings; and 9- and 10-membered heteroaryl are 6,5-fused and 6,6-fused bicyclic rings,

respectively, wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O and S atoms both are present, the O and S atoms are not bonded to each other;

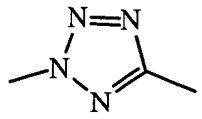
wherein with any $(C_1\text{-}C_6$ alkyl$)_2$-N group, the $C_1\text{-}C_6$ alkyl groups may be optionally taken together with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocycloalkyl; and

wherein each group and each substituent recited above is independently selected.

2. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein V^1 is



3. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein V^1 is



4. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Q is $N(R^6)C(O)$.

5. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Q is C≡C.

6. The compound according to any one of Claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein at least one of R^1 and R^2 is independently selected from:

Phenyl-$(C_1\text{-}C_6$ alkylenyl); and

Substituted phenyl-$(C_1\text{-}C_6$ alkylenyl);

wherein each group and each substituent is independently selected.

7. The compound according to according to any one of Claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein at least one of R^1 and R^2 is independently selected from:

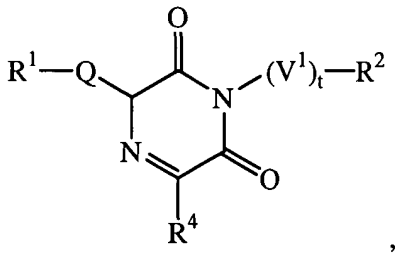
5-, 6-, 9-, and 10-membered heteroaryl-(C_1-C_6 alkylenyl); and

Substituted 5-, 6-, 9-, and 10-membered heteroaryl-(C_1-C_6 alkylenyl);

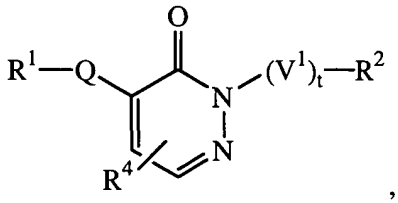
wherein each heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C_1-C_6 alkyl), and 4 N, and 5- and 6-membered heteroaryl are monocyclic rings and 9- and 10-membered heteroaryl are 6,5-fused and 6,6-fused bicyclic rings, respectively, wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O and S atoms both are present, the O and S atoms are not bonded to each other; and

wherein each group and each substituent is independently selected.

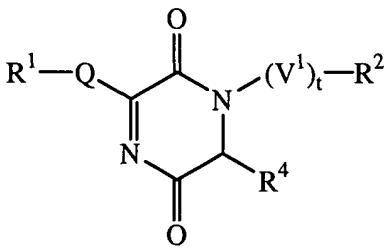
8. A compound of Formula II, III, IV, V, or VI



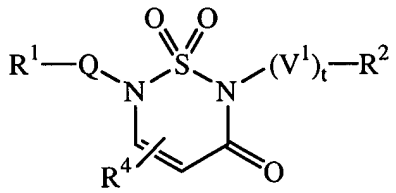
, II



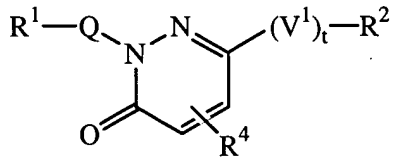
, III



, IV



, V



and , VI

or a pharmaceutically acceptable salt thereof.

9. The compound of Formula II according to Claim 8, selected from:

4-[5-(3-Benzylcarbamoyl-2,6-dioxo-3,6-dihydro-2H-pyrazin-1-yl)-tetrazol-2-yl]-benzoic acid;

4-(5-{2,6-Dioxo-3-[(pyridin-4-ylmethyl)-carbamoyl]-3,6-dihydro-2H-pyrazin-1-yl}-tetrazol-2-yl)-benzoic acid;

4-[3-(3-Benzylcarbamoyl-2,6-dioxo-3,6-dihydro-2H-pyrazin-1-yl)-prop-2-ynyl]-benzoic acid;

4-(3-{2,6-Dioxo-3-[(pyridin-4-ylmethyl)-carbamoyl]-3,6-dihydro-2H-pyrazin-1-yl}-prop-2-ynyl)-benzoic acid;

4-{2-[2,6-Dioxo-3-(3-phenyl-prop-1-ynyl)-3,6-dihydro-2H-pyrazin-1-yl]-oxazol-5-yl}-benzoic acid;

4-{2-[3-(3-Imidazol-1-yl-prop-1-ynyl)-2,6-dioxo-3,6-dihydro-2H-pyrazin-1-yl]-oxazol-4-yl}-benzoic acid;

4-{3-[2,6-Dioxo-3-(3-phenyl-prop-1-ynyl)-3,6-dihydro-2H-pyrazin-1-yl]-prop-2-ynyl}-benzoic acid;

4-{3-[3-(3-Imidazol-1-yl-prop-1-ynyl)-2,6-dioxo-3,6-dihydro-2H-pyrazin-1-yl]-prop-2-ynyl}-benzoic acid;

4-({[2,6-Dioxo-3-(5-phenyl-oxazol-2-yl)-3,6-dihydro-2H-pyrazine-1-carbonyl]-amino}-methyl)-benzoic acid;

4-{3-[2,6-Dioxo-3-(5-phenyl-oxazol-2-yl)-3,6-dihydro-2H-pyrazin-1-yl]-prop-2-ynyl}-benzoic acid;

4-{5-[2,6-Dioxo-3-(4-phenyl-oxazol-2-yl)-3,6-dihydro-2H-pyrazin-1-yl]-tetrazol-2-yl}-benzoic acid; and

4-{3-[2,6-Dioxo-3-(4-phenyl-oxazol-2-yl)-3,6-dihydro-2H-pyrazin-1-yl]-prop-2-ynyl}-benzoic acid;

or a pharmaceutically acceptable salt thereof.

10. The compound of Formula III according to Claim 8, selected from:

4-[5-(5-Benzylcarbamoyl-6-oxo-6H-pyridazin-1-yl)-tetrazol-2-yl]-benzoic acid;

4-(5-{6-Oxo-5-[(pyridin-4-ylmethyl)-carbamoyl]-6H-pyridazin-1-yl}-tetrazol-2-yl)-benzoic acid;

4-[3-(5-Benzylcarbamoyl-6-oxo-6H-pyridazin-1-yl)-prop-2-ynyl]-benzoic acid;

4-(3-{6-Oxo-5-[(pyridin-4-ylmethyl)-carbamoyl]-6H-pyridazin-1-yl}-prop-2-ynyl)-benzoic acid;

4-{2-[6-Oxo-5-(3-phenyl-prop-1-ynyl)-6H-pyridazin-1-yl]-oxazol-5-yl}-benzoic acid;

4-{2-[5-(3-Imidazol-1-yl-prop-1-ynyl)-6-oxo-6H-pyridazin-1-yl]-oxazol-4-yl}-benzoic acid;

4-{3-[6-Oxo-5-(3-phenyl-prop-1-ynyl)-6H-pyridazin-1-yl]-prop-2-ynyl}-benzoic acid;

4-{3-[5-(3-Imidazol-1-yl-prop-1-ynyl)-6-oxo-6H-pyridazin-1-yl]-prop-2-ynyl}-benzoic acid;

4-({[6-Oxo-5-(5-phenyl-oxazol-2-yl)-6H-pyridazine-1-carbonyl]-amino}-methyl)-benzoic acid;

4-{3-[6-Oxo-5-(5-phenyl-oxazol-2-yl)-6H-pyridazin-1-yl]-prop-2-ynyl}-benzoic acid;

4-{5-[6-Oxo-5-(4-phenyl-oxazol-2-yl)-6H-pyridazin-1-yl]-tetrazol-2-yl}-benzoic acid; and

4-{3-[6-Oxo-5-(4-phenyl-oxazol-2-yl)-6H-pyridazin-1-yl]-prop-2-ynyl}-benzoic acid;

or a pharmaceutically acceptable salt thereof.

11. A pharmaceutical composition, comprising a compound according to Claim 1, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

12. The pharmaceutical composition according to Claim 11, comprising a compound according to Claim 9 or 10, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

13. A method for treating osteoarthritis or rheumatoid arthritis, comprising administering to a patient suffering from osteoarthritis or rheumatoid arthritis a nontoxic effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt thereof.

14. The method according to Claim 13, wherein the compound administered is a compound according to Claim 9 or 10, or a pharmaceutically acceptable salt thereof.